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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,420	06/09/2006	Shifu Zhao	JEEKP103US	7408

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
08/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/582,420	ZHAO ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 9-20* is/are pending in the application.

4a) Of the above claim(s) *12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9-11 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received May 27, 2008.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 2, 8 are canceled. Claims 12-15 are withdrawn. Claims 1, 3-7, 9-11, 16-20 are currently under examination.

Priority: The priority date is December 11, 2003.

Objections and Rejections

Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 17 does not properly limit the parent claim but merely refers to it (claim 1).

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 17 remains rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 17, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the

claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, i.e. by insertion of "isolated" or purified." See MPEP 2105.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 9-11, 16-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to hGlyrichin and mGlyrichin or fragments and derivatives thereof, that have antibacterial properties. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As stated above, hGlyrichin and mGlyrichin or fragments and derivatives thereof, that have antibacterial properties. However, the skilled artisan cannot necessarily envision the detailed structures of ALL of the derivatives and/or fragments of hGlyrichin and/or mGlyrichin that have

the same functional activity as the wild-type hGlyrichin and/or mGlyrichin because nowhere in the specification is it described which amino acids are even essential and critical for the wild-type protein to maintain its functionality, and therefor conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Despite antibacterial peptides being known in the art, the instant specification does not disclose any structural similarity to foster that function. Further, there does not appear to be an adequate description in the specification and/or sequence listing of mouse Glyrichin (mGlyrichin). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

In their remarks, Applicants assert claim 1 has been amended to recite that in addition to SEQ ID NO: 1, up to 20 amino acids may be deleted or substituted and/or up to 20 amino acids can be added to the amino- or carboxyl-terminus. A claim to a genus is appropriate if supported by a sufficient number of specific species disclosed in the Application. Applicants' assert that here, various species are disclosed in the Application, for example Table 1, lists possible substitutions that were possessed by Applicants at time of filing and are fully expected by those with ordinary skill in the art to have antimicrobial function; further the Application additionally teaches that it is preferred for the homology to remain with 90% of the original SEQ ID NO: 1 or corresponding DNA sequence SEQ ID NO: 2 (specification p. 5, lines 6-11). Applicant's arguments have been fully considered but they are not persuasive.

Instant claim 1 is drawn to an amino acid sequence of SEQ ID NO: 1 or a protein having antibacterial activities having SEQ ID NO: 1 with 1-20 amino acid residues deleted, inserted, and/or substituted. The instant specification appears to disclose human and mouse Glyrichin, i.e. SEQ ID NO: 1, having antibacterial activity. There are no other drawings or structural formulas disclosed that show a sequence having 90% identity to SEQ ID NO: 1. As noted by Applicants, Table 1 lists representative and preferred substitutions that one of ordinary skill would recognize can be substituted to obtain a polypeptide having at least 90% sequence identity with SEQ ID NO: 1. However, there is no teaching of which 10% of the amino acids can vary from SEQ ID NO: 1 and still result in a protein that retains antimicrobial function. The specification does not appear to provide clear guidance as to which amino acid residues within SEQ ID NO: 1 should be altered, i.e. conservative/non-conservative substitutions, deletions, insertions to generate a derivative of SEQ ID No: 1 that has 90% sequence identity and antimicrobial function. It is known in the art that an amino acid sequence identity of 50% does not guarantee structural similarity (Yuan et al. 1998 Proteins 30: 136-143), and that even a single point mutation in a polypeptide sequence can lead to surprising alteration in protein structure and activity (Sergel et al. 2000 J Virol 74: 5101-5107).

The guidelines for the examination of patent applications under 35 U.S.C. 112, first paragraph, written description requirement, make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or

by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the genus (Federal Register Vol. 66, No. 4 pages 1099-111, January 5, 2001). As discussed above, the relevant structural features that are to be used in identifying structurally similar proteins are not well defined. In view of this, one of ordinary skill in the art would reasonably conclude that the disclosure fails to provide that general similarity of structure confers said antimicrobial activity. Thus, Applicants were not in possession of the claimed genus of all derivatives of SEQ ID NO: 1 having 90% sequence identity. Applicant is directed to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, § 1 Written Description Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-7, 9-11, 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is directed to an isolated human Glyrichin (hGlyrichin) or isolated mouse Glyrichin (mGlyrichin). The claim is indefinite because it is unclear what "human" Glyrichin is other than SEQ ID NO: 1. The claim also recites variants of SEQ ID NO: 1 but is also directed to a mouse or human sequence of Glyrichin. Further clarification is requested.

Claims 3-7, 9-11, 16-20 are included in this rejection because they are dependent on the above claims and fail to cure the defect.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al. (WO 9943802). Kato et al. teach a protein comprising an amino acid sequence depicted as SEQ ID NO: 3, which has 100% sequence identity to instant SEQ ID NO: 1 (p. 60). Kato et al. also teach a DNA depicted as SEQ ID NO: 10, which essentially has 100% sequence identity to instant SEQ ID NO: 2, expression vectors comprising said DNA, and eukaryotic cells transformed with said DNA (p. 60; claims 17-18).

Claims 17-18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al. because claim 17 is merely directed to the gene encoding the isolated protein. There is not an additional requirement about an expression construct in the claim or in claim 18, which is dependent on claim 17.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-7, 9-10, 16, 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (WO 9943802; previously cited). Kato et al. disclose a protein comprising an

amino acid sequence depicted as SEQ ID NO: 3, which has 100% sequence identity to instant SEQ ID NO: 1 (p. 60). Kato et al. also disclose a DNA depicted as SEQ ID NO: 10, which essentially has 100% sequence identity to instant SEQ ID NO: 2, expression vectors comprising said DNA, and eukaryotic cells transformed with said DNA (p. 60). Kato et al. further disclose derivatives and/or fragments to said protein and DNA (p. 7, 9, 56). Additionally, Kato et al. disclose bacteria can be engineered to contain said DNA (p. 4-5 lines 32-3). On page 4, Kato et al. disclose that the protein of interest can be expressed by using prokaryotic cells, i.e. *E. coli*, and eukaryotic cells, i.e. yeast. Kato et al. do not explicitly teach the expression of the protein of interest in a prokaryotic system and/or yeast. Such expression is required to produce the claimed protein due to glycosylation patterns in different expression systems.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to express the polypeptide of SEQ ID NO: 1 (Glyrichin) in a prokaryotic system or yeast and in order to obtain the isolated polypeptide because Kato et al. disclose Glyrichin protein can be expressed in prokaryotic and eukaryotic systems (claims 1, 3-7, 9-11, 16, 19-20). One would have had a reasonable expectation of success to make the claimed proteins due to the high level of skill in the art of yeast protein expression.

In their remarks, Applicants assert Kato et. al. appears to disclose expression of SEQ ID NO:3 (Kato et al) in Saos-2 cells (Kato et al Table 1) for the purposes of producing antibodies having affinity to the same. Immunological responsiveness is highly dependent upon post-translational modification (i.e. glycosylation) that is unique to the *in vivo* expression system through which recombinant proteins are produced. Proteins produced in prokaryotic systems

and by *in vitro* methods lack such post-translational modifications all together. Applicants further assert that Claim 1 has been amended to recite the expression of SEQ ID NO: 1 in one or more of prokaryotic systems, yeast, and by *in vitro* methods. Kato et al only teaches production of the SEQ ID NO: 3 in Saos-3. Such peptides produced in Sao-2 will have different glycosylation and other post-translational modifications from the peptide of claim 1, as amended. Applicant's arguments have been fully considered but they are not persuasive.

The rejection of the claims under 35 U.S.C. 102(b) as being anticipated by Kato et al. has been withdrawn. However, the Kato et al. reference is still believed to be relevant art under 103(a), as noted above.

The scope of claim 11, i.e. a method of using Glyrichin for an antibacterial purpose, appears to be free of art.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 1, 2008

/Kathleen Kerr Bragdon/

Supervisory Patent Examiner, Art Unit 1656